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# Efficacy of Octreotide Acetate in Treatment of Severe Postgastrectomy Dumping Syndrome

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The present study evaluates the acute and chronic use of a long-acting somatostatin analog, octreotide acetate, in the treatment of patients with severe postgastrectomy dumping syndrome. In the acute phase, 10 patients with severe dumping were studied over 2 consecutive days before and for 3 hours after the ingestion of a 'dumping breakfast' in a randomized double-blind fashion. On one day octreotide (100 µg) was given subcutaneously 30 minutes before the test meal and on the other day an equal volume of vehicle was injected. An additional group of six postgastrectomy patients without dumping were studied in a similar fashion and these acted as controls. During placebo treatment the test meal resulted in an immediate increase ( $p < 0.01$ ) in the pulse rate and in plasma levels of glucose, glucagon, pancreatic polypeptide, neurotensin, and insulin. Similar changes were seen in the control group with respect to placebo; however glucagon and neurotensin ( $p < 0.05$ ) did not show the same magnitude of increase as seen with placebo. Treatment with octreotide acetate prevented the development of both vasomotor and gastrointestinal symptoms and completely ablated all of the above responses in plasma peptides. These changes were associated with complete ablation of diarrhea ( $p < 0.001$ ). Pretreatment with octreotide acetate completely suppressed the rise in plasma insulin response to the meal and this ablated the late hypoglycemia of dumping. Treatment with octreotide acetate resulted in delayed gastric emptying and transit time ( $578 \pm 244$  minutes) versus  $76 \pm 23$  minutes with placebo and  $125 \pm 36$  minutes in controls ( $p < 0.05$ ). Chronic daily treatment with octreotide acetate resulted in minimal side effects. These patients demonstrated a stable fasting plasma glucose, normal liver function tests, and an average weight gain of 11% during a 12-month period. In addition most patients were able to resume employment. The long-acting somatostatin analog, octreotide acetate, is highly effective in preventing the

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development of symptoms of severe dumping syndrome, both vasomotor and gastrointestinal.

**T**HE DUMPING SYNDROME, DESCRIBED by Mix in 1922,<sup>1</sup> results from the alteration, ablation, or bypass of the pyloric sphincter mechanism. Nearly one half of all patients who undergo gastric operations develop symptoms of dumping but less than 5% of these patients have severe symptoms requiring other forms of treatment after dietary management has failed.<sup>2</sup> Early dumping symptoms typically are observed within 15 to 30 minutes after the ingestion of a high carbohydrate meal. The syndrome is characterized by sudden onset of vasomotor symptoms, such as diaphoresis, palpitations, weakness, faintness, and an intense desire to lie down. The gastrointestinal symptoms are more distressing with abdominal bloating, cramping, and profound diarrhea usually within 1 hour after a meal. Late dumping symptoms occur much less frequently than early dumping but can occur in combination with early dumping. These symptoms, including perspiration, rapid heart rate, mental confusion, and syncope occur 1 to 2 hours after a meal and are thought to be the result of insulin-induced hypoglycemia.

The range of symptoms in patients with dumping syndrome vary widely from minimal symptoms only with certain foods to profound dumping with almost all foods. Severe symptoms result in marked weight loss, fear of eating, fear of leaving the house, and, in most cases, the inability to work full-time.<sup>3</sup> Patients with severe dumping

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have been associated with a significant psychologic overlay<sup>4</sup> causing a magnification of symptoms. However these patients are now being recognized as having other physiologic reasons for the symptoms of the dumping syndrome.<sup>5-9</sup>

The exact etiology of dumping is unknown. The release of several humoral agents is increased in patients with dumping and not in asymptomatic postgastrectomy patients, thus implicating them in the pathogenesis of the syndrome. The agents include glucagon, neurotensin,<sup>5</sup> vasoactive intestinal peptide,<sup>6</sup> serotonin,<sup>7</sup> and bradykinin.<sup>8</sup> We and others<sup>10-12</sup> hypothesized that if these factors or hormones could be inhibited with somatostatin it might be possible to ablate the symptoms of dumping. Octreotide acetate (Sandostat, Sandoz, East Hanover, NJ), is a somatostatin analogue that has a longer half-life, which allows administration *via* a subcutaneous route. In the present study, octreotide acetate was evaluated in an acute double-blind randomized prospective trial in alleviating the symptoms associated with severe dumping syndrome. This study also examines the efficacy of chronic treatment (up to 15 months) of patients with severe dumping syndrome.

### Materials and Methods

Patients with severe dumping syndrome were selected by a careful history of their symptom complex. Selection included failure of dietary manipulation, weight loss of more than 10% of body weight, and symptoms causing a significant alteration in lifestyle. The symptoms included faintness, weakness, diaphoresis, palpitations, abdominal

bloating, cramping, nausea, and diarrhea (more than 5 episodes per day). The selection process also included reproducing the symptoms after the ingestion of a solid 'dumping breakfast'; this consisted of a 750-kcal solid meal with 21 g protein, 30 g fat, and 99 g carbohydrate. At the end of this trial, the patients were asked to rank their symptoms on a severity scale from 0 (no symptoms) to 10 (the most severe symptoms). The efficacy of this scale was tested repeatedly (on 3 to 7 occasions) for each subject, with an intraindividual variability of  $2.5\% \pm 0.1\%$ . Only patients with severity scores more than 7 following the 'dumping breakfast' trial were invited to participate in the present study. Eight patients had severe symptoms of early dumping with no late dumping and two patients had symptoms suggestive of both severe early and late dumping (Table 1). Six postgastrectomy patients with no symptoms of dumping also were studied to measure gastric emptying and hormonal response and served as controls.

All patients signed an informed consent form before entering the study. The protocol was approved by the Institutional Committee for the Protection of Human Subjects at Vanderbilt University. The patients were studied on two consecutive days in the Vanderbilt Clinical Research Center. Each patient was fasted overnight and then studied, before and for 3 hours after the ingestion of a high caloric 'dumping breakfast' meal. On one day, 100  $\mu\text{g}$  of octreotide acetate was given subcutaneously 30 minutes before the test meal (denoted octreotide trial) and on the other day an equal volume of vehicle (denoted placebo trial) was injected. All patients were studied in the supine position. The order of the trials were assigned in a randomized double-blind fashion, both to the inves-

TABLE 1. Patient Characteristics

Patient	Age (years)	Sex	Operative Procedure	Duration of Symptoms (years)	Percentage of Body Weight Loss	Type of Dumping
1	34	M	Total gastrectomy	12	25	Early + late
2	60	F	Vagotomy and antrectomy + Billroth I	4	16	Early
3	50	F	Vagotomy and antrectomy + Billroth I	1	15	Early
4	35	F	Vagotomy and antrectomy + Roux-en-Y	8	50	Early + late
5	62	F	Vagotomy and antrectomy + Billroth I	2	24	Early
6	46	M	Vagotomy and antrectomy + Billroth I	7	44	Early
7	33	F	Vagotomy and antrectomy + Billroth I	4	43	Early
8	70	M	Vagotomy and antrectomy + Billroth II	34	10	Early
9	41	M	Vagotomy and antrectomy + Roux-en-Y	3	33	Early
10	61	F	Vagotomy and antrectomy + Billroth I	14	25	Early

M, male; F, female.

tigator and the patient. Blood samples were obtained from an indwelling intravenous catheter every 15 to 30 minutes during the study period for the determination of plasma glucose and intestinal peptides. Blood pressure and pulse rate were monitored continuously throughout the study period. At the conclusion of the study the patients were asked to rank their symptoms again.

At the end of the second study day, the blinding code was broken and the patients were informed of the outcome. All patients were placed on chronic maintenance therapy with the somatostatin analogue, with doses varying from 30 to 70  $\mu\text{g}$  subcutaneously taken three to four times each day. On three occasions the analog was given 30 minutes before each meal and also was given at bedtime.

Analysis of plasma glucose was performed using the glucose oxidase method. Plasma concentrations of vasoactive intestinal peptide,<sup>13</sup> pancreatic polypeptide,<sup>13</sup> motilin,<sup>14</sup> insulin,<sup>15</sup> glucagon,<sup>16</sup> and gastrin<sup>17</sup> were measured using established radioimmunoassay methods. Plasma concentrations of neurotensin were determined in unextracted plasma by a modification of a previously described assay.<sup>18</sup> All plasma samples for measurement of a given peptide were tested in a single assay; the intra-assay coefficient of variation was less than 6% for all assays.

Gastric emptying was assessed in five dumping and five control patients using standard solid-phase Technetium<sup>99m</sup>-labeled scrambled eggs as the test meal. Gastric emptying was quantitated as the time it took for one half of the radiolabel to leave the stomach. The normal  $T_{1/2}$  of gastric emptying is 60 to 90 minutes.

Results are expressed as the mean  $\pm$  standard error of the mean (SEM). Statistical analysis was performed using Student's paired *t* test and analysis of variance, where applicable.

## Results

### *Patient Characteristics (Table 1)*

Ten patients (four men and six women) were included in the study. The mean age was 49 years (range, 33 to 70 years). All patients had previous gastric surgery. Vagotomy and antrectomy was performed in nine of the patients; six had Billroth I anastomosis, one had a Billroth II anastomosis, and two had Roux-en-Y-gastrojejunostomies. One patient had a total gastrectomy. All manifested dumping symptoms that have lasted from 1 to 34 years, with a mean of 8.9 years. Nine of the ten patients had significant weight loss (15% or more) since the onset of dumping symptoms. In the control group, six patients (three men and three women) were studied. Mean age was 54 years (range, 53 to 69 years). All had previous gastric surgery. Vagotomy and antrectomy was performed in five patients; three had Roux-en-Y-gastrojejunostomies,

one had a Billroth I, and one had a Billroth II reconstruction. One patient had a total gastrectomy. No dumping symptoms were present in any of these postgastrectomy patients.

### *Pulse Rate and Blood Pressure (Fig. 1)*

A significant increase in pulse rate was seen during the placebo trial within 15 minutes of meal consumption ( $p < 0.01$ ). This effect persisted until the end of the 3-hour experimental period when the pulse rate returned to basal levels. Octreotide acetate completely ablated the increase in pulse rate. Neither trial showed any significant change in the systolic, diastolic, or mean arterial blood pressures after the test meal (data not shown).

### *Dumping Symptoms (Fig. 2)*

The severity score of dumping symptoms during the placebo trial was  $8.5 \pm 0.5$ . When octreotide acetate was given before the meal, we observed a marked reduction in the symptom severity score to  $1.7 \pm 0.5$  ( $p < 0.001$ ). Within 3 hours of meal ingestion, 8 of the 10 patients receiving the placebo trial developed severe diarrhea, with a frequency of 1.7 episodes (range, 2 to 5 episodes). None of the patients treated with octreotide acetate developed diarrhea ( $p < 0.001$ ). In the two patients with late dumping, their symptoms were completely ablated with octreotide acetate treatment. The only adverse effects of octreotide was mild transient (lasting an average of 5 minutes) abdominal cramping noted in four patients, which occurred shortly after injection of the drug.

### *Plasma Glucose Levels (Fig. 3)*

Basal plasma glucose levels were identical in the dumping and nondumping postgastrectomy subjects and averaged  $86 \pm 2$  mg/dL. During the placebo trial, plasma glucose rose to peak levels of  $190 \pm 18$  mg/dL within 45 minutes and returned to basal levels by 120 minutes. The increase in plasma glucose in the octreotide trial was much greater ( $p < 0.01$ ), reaching peak levels of  $277 \pm 25$  mg/dL by 75 minutes and decreased to  $183 \pm 14$  mg/dL by the end of the experimental period. The two patients with late dumping symptoms manifested profound hypoglycemia, with an average nadir plasma glucose level (44 mg/dL) at 90 minutes; this was ablated with pretreatment with octreotide acetate.

### *Plasma Insulin and Glucagon Levels*

During the placebo trial plasma insulin levels increased to peak levels 10 to 12 times basal in response to the meal, as shown in Figure 4; the peak levels coincided with those of plasma glucose. The increase in plasma insulin was completely blocked by octreotide acetate pretreatment ( $p$

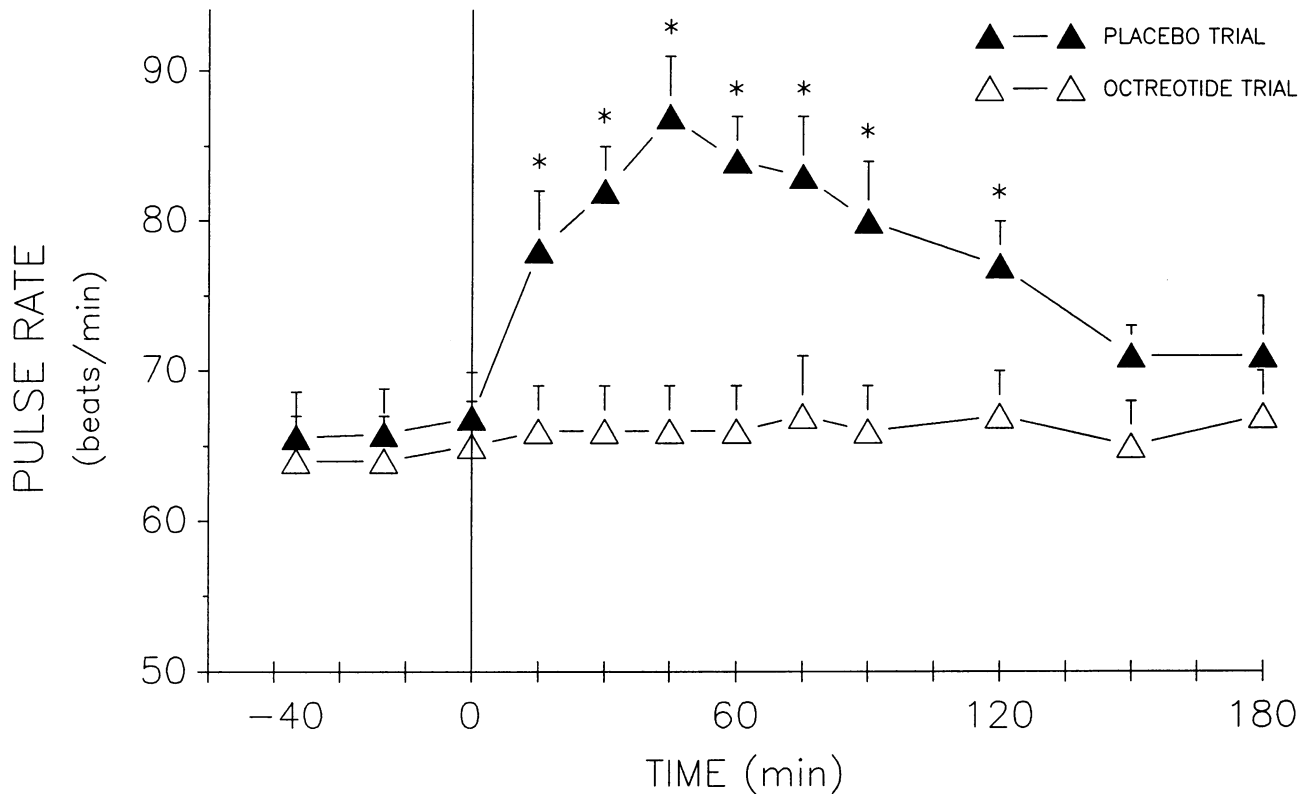


FIG. 1. Pulse rate (beats/minute) in 10 subjects known to have severe dumping symptoms, before and after a high carbohydrate breakfast given at 0 minutes and consumed within 15 minutes. Thirty minutes before the meal, the patients received a subcutaneous injection of 100  $\mu$ g of octreotide acetate (open triangles), or a vehicle (closed triangles). (\* Denotes differences between the group at  $p < 0.01$ .)

< 0.01). Changes in plasma glucagon paralleled those of insulin and, as shown in Figure 5, were inhibited by octreotide acetate treatment. The control group showed a similar increase in plasma insulin as the patients while receiving the placebo trial. In addition they manifested a

very slight rise in plasma glucagon but not to the same magnitude as that seen in the patients during the placebo trial ( $p < 0.05$ ).

*Intestinal Peptides*

Plasma levels of the octreotide acetate reached peak values of  $4698 \pm 821$  pg/mL within 10 minutes of a subcutaneous injection of 100  $\mu$ g, as shown in Figure 6. Subsequently the decrease in plasma levels of the drug followed a first-order kinetics with drug levels still exceeding 1000 pg/mL at the end of the 3-hour study period. The half-life of the drug calculated from Figure 6 was 90 minutes.

Five intestinal peptides were measured in this study: gastrin, neurotensin, motilin, pancreatic polypeptide, and vasoactive intestinal peptide (VIP). The levels of neurotensin and pancreatic polypeptide were significantly elevated during the placebo trial, as shown in Figure 7. The increase in both peptides, however, was abolished during the octreotide trial groups ( $p < 0.05$ ). Following the breakfast meal, the subjects in the control group showed significant increases in the plasma levels of neurotensin and pancreatic polypeptide. The increase in neurotensin was blunted when compared to the levels seen in the

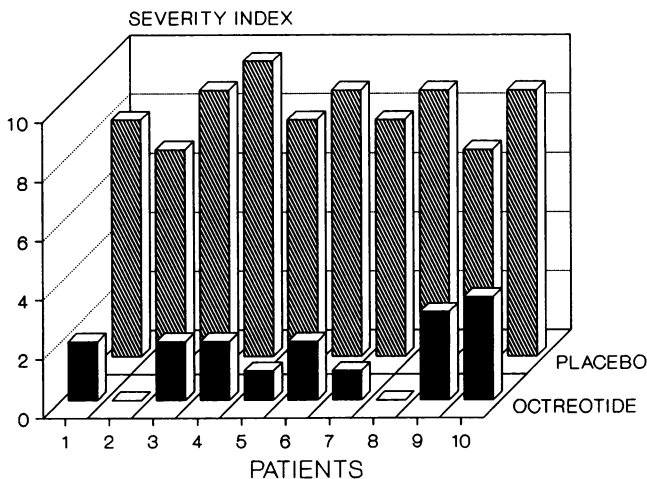


FIG. 2. Severity score for dumping symptoms of each of the 10 patients described in Figure 1, treated with octreotide (closed bars) or placebo (hatched bars). A score of zero denotes no symptoms and a score of 10 denotes severe symptoms.

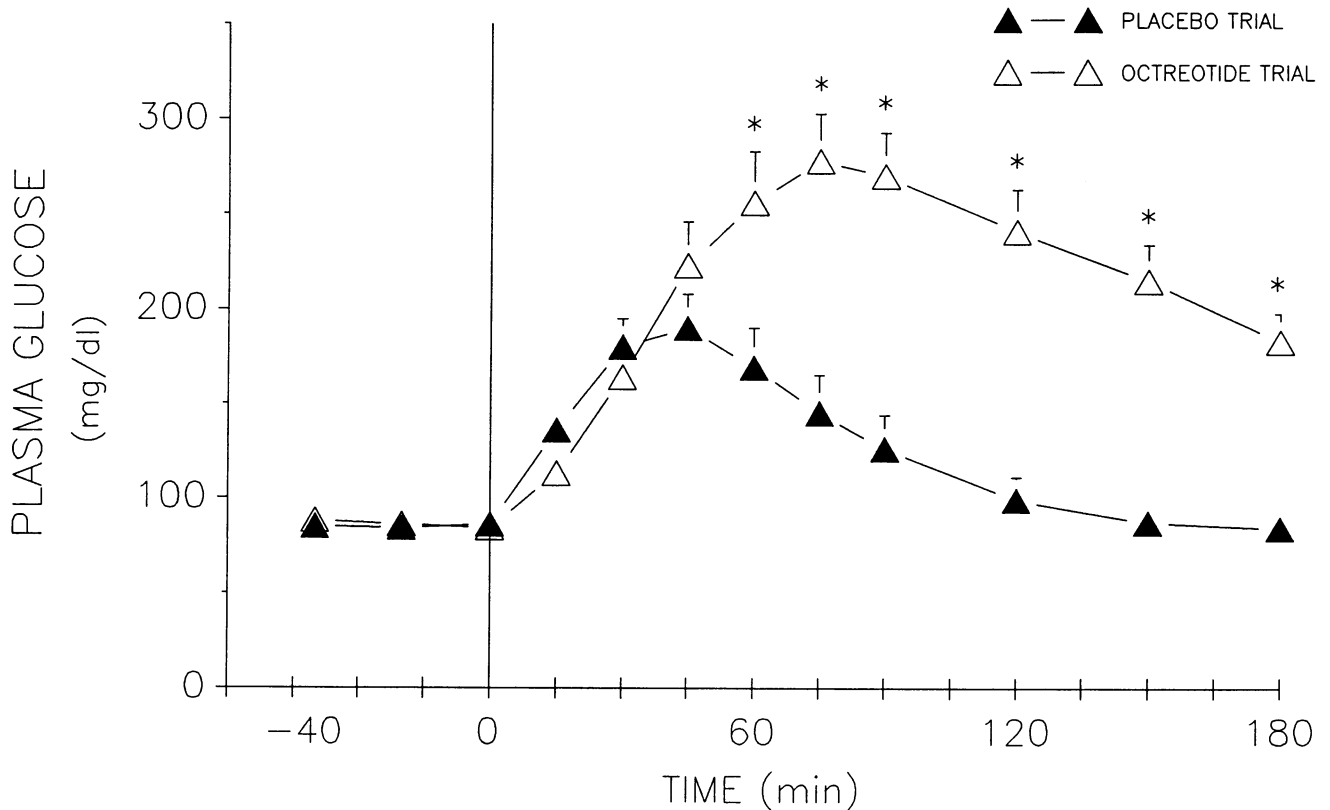


FIG. 3. Plasma glucose concentrations after a high carbohydrate meal in patients pretreated with (open triangles) octreotide or with placebo (closed triangles). The patients were described in Figure 1. (\* Denotes difference between groups at  $p < 0.01$ .)

dumping patients during placebo trial and were significantly higher than those seen in the patients during the octreotide trial. Plasma levels of gastrin, motilin, and vasoactive intestinal peptide showed no significant changes in any of the groups (data not shown) in response to the meal.

#### Gastric Emptying (Table 2)

Gastric emptying was assessed by Technetium<sup>99m</sup>-labeled scrambled eggs in five patients with and without treatment with octreotide. The mean emptying time during the placebo trial averaged  $76 \pm 23$  minutes, with a wide range of variability (21 to 150 minutes). These values were not significantly different from those seen in the nondumping patients or from normal controls ( $125 \pm 32$  minutes). This is attributed to the fact that the radiolabeled scrambled egg meal given did not contain high amounts of carbohydrates. Interestingly, in three subjects (3, 4, and 5) who manifested normal pretreatment retention times,

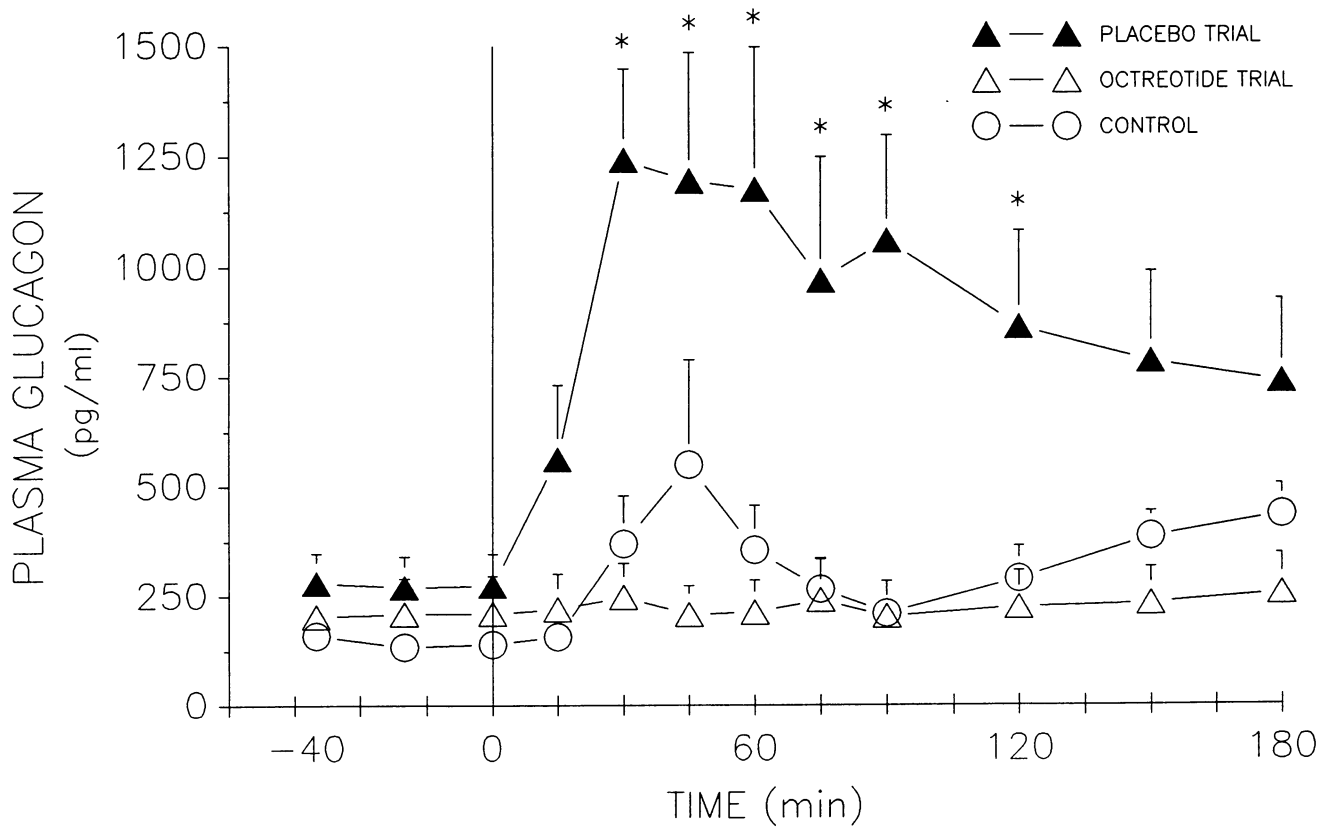
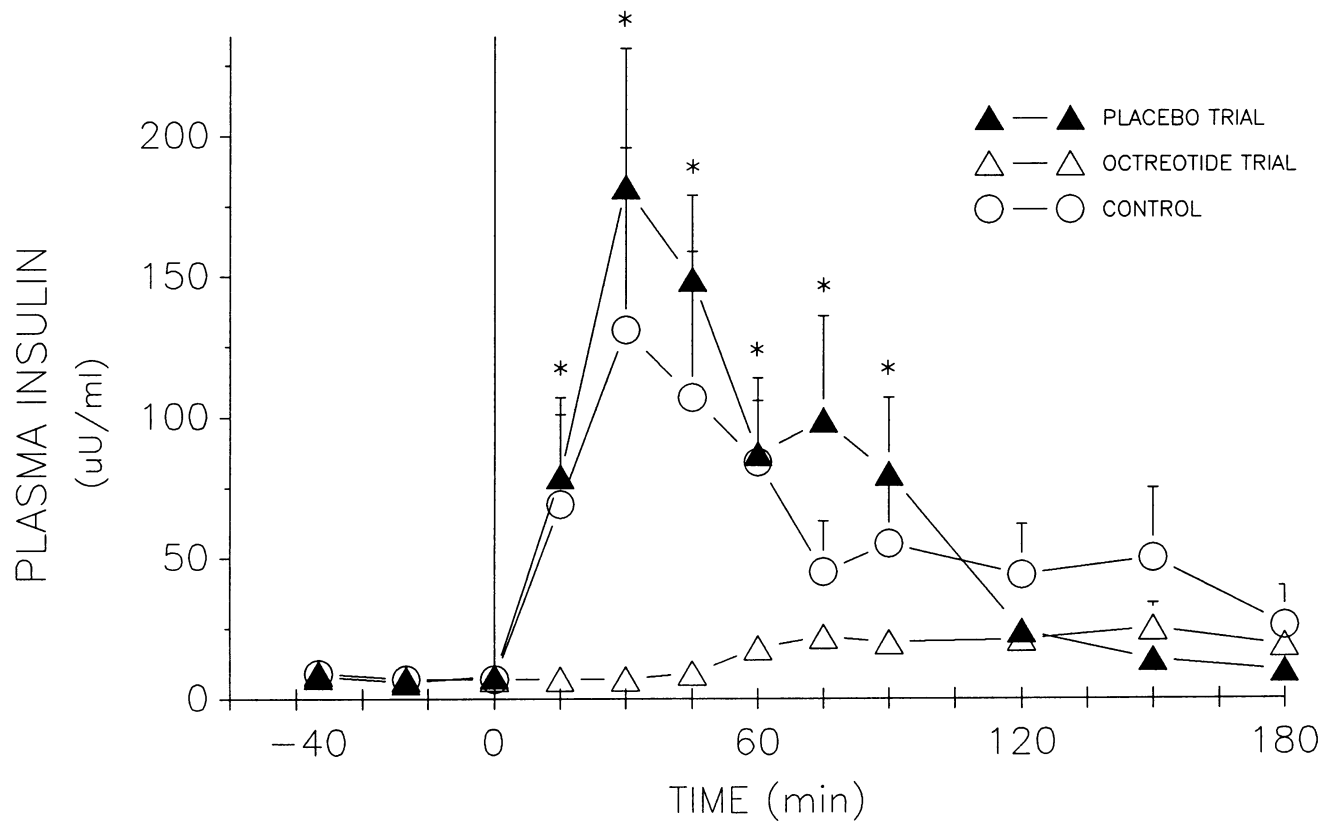
emptying of gastric contents was associated with significant rush of food through the upper gastrointestinal tract, which was followed by diarrhea. In each of the patients studied, pretreatment with octreotide acetate prolonged the gastric emptying time ( $p < 0.05$ ).

#### Long-term Studies

As already noted acute treatment with octreotide acetate resulted in a significant postprandial increase in plasma glucose levels and a blunted response in plasma insulin. These findings prompted us to investigate the long-term sequelae of octreotide acetate and particularly whether the long-term use of this drug is associated with a diabetic-like state. The subjects were followed monthly and biochemical parameters obtained at 3 and 15 months are shown in Table 3. Long-term treatment with octreotide acetate was associated with stable fasting plasma glucose levels, normal liver enzymes, and a significant weight gain. Since beginning chronic treatment with octreotide acetate,

FIG. 4. (Top) Plasma insulin levels for the same patients described in Figure 1 while pretreated with octreotide (open triangles) or with placebo (closed triangles). (\* Denotes difference between  $\blacktriangle$  and  $\triangle$ ,  $p < 0.01$ .)

FIG. 5. (Bottom) Plasma glucagon levels for the same patients described in Figure 1 with octreotide pretreatment (open triangles) or with placebo (closed triangles). (\* Denotes difference between  $\blacktriangle$  and  $\triangle$ ,  $p < 0.01$  and  $\blacktriangle$  and  $\circ$ ,  $p < 0.05$ .)



seven patients who were unemployed because of symptoms before the study have returned to work.

### Discussion

The results of this double-blind prospective study show conclusively that the somatostatin analogue, octreotide acetate, is effective in preventing early dumping symptoms after ingestion of a high carbohydrate meal and prevented the appearance of hypoglycemia, a characteristic sign of late dumping symptoms. The present study also shows conclusively that long-term treatment with octreotide acetate (up to 15 months) was safe and resulted in significant weight gain and improved symptomatology. The overall well-being of these patients improved drastically.

The etiology of dumping syndrome remains largely unknown. Several theories have been proposed, and the most popular is the hyperosmolar load theory.<sup>19</sup> This theory states that the loss of the pyloric sphincter results in enhanced gastric emptying with rapid delivery of the hyperosmolar meal into the small intestine. This, in turn, causes a marked shift of extracellular fluid into the lumen, resulting in hemoconcentration and presumably a mild shocklike state.<sup>20</sup> It is uncertain whether the development of symptoms, both vasomotor and gastrointestinal, in

these patients was directly related to the shocklike state or was the result of increased release of humoral factors. Johnson et al.<sup>9</sup> suggested that a transfusible factor was responsible for the development of dumping symptoms. Since that time a number of other investigators have implicated a variety of gastrointestinal hormones as the etiologic agent(s) in the dumping syndrome. These developments have lead us and others<sup>10-12</sup> to postulate that the use of somatostatin, which inhibits hormonal secretion, can ablate dumping symptoms.

Somatostatin, first discovered in the hypothalamic tissues, and presently known to be produced in several other tissues, including the antral mucosa, duodenum, pancreas, and testes has been shown to be a very potent inhibitor of the release of many peptides, primarily those formed by the gastropancreatic tissues.<sup>21</sup> Administration of somatostatin for the treatment of the dumping syndrome has, however, encountered limited success.<sup>10,11</sup> This was mainly due to the short half-life (1 to 2 minutes) of the peptide, which necessitates a continuous intravenous infusion to maintain adequate drug levels in the blood. Octreotide acetate (Sandostatin, Sandoz, East Hanover, NJ), described in 1982, is an octapeptide analogue of cyclic somatostatin. The chief advantage of the analogue over the natural compound, cyclic somatostatin, resides in its

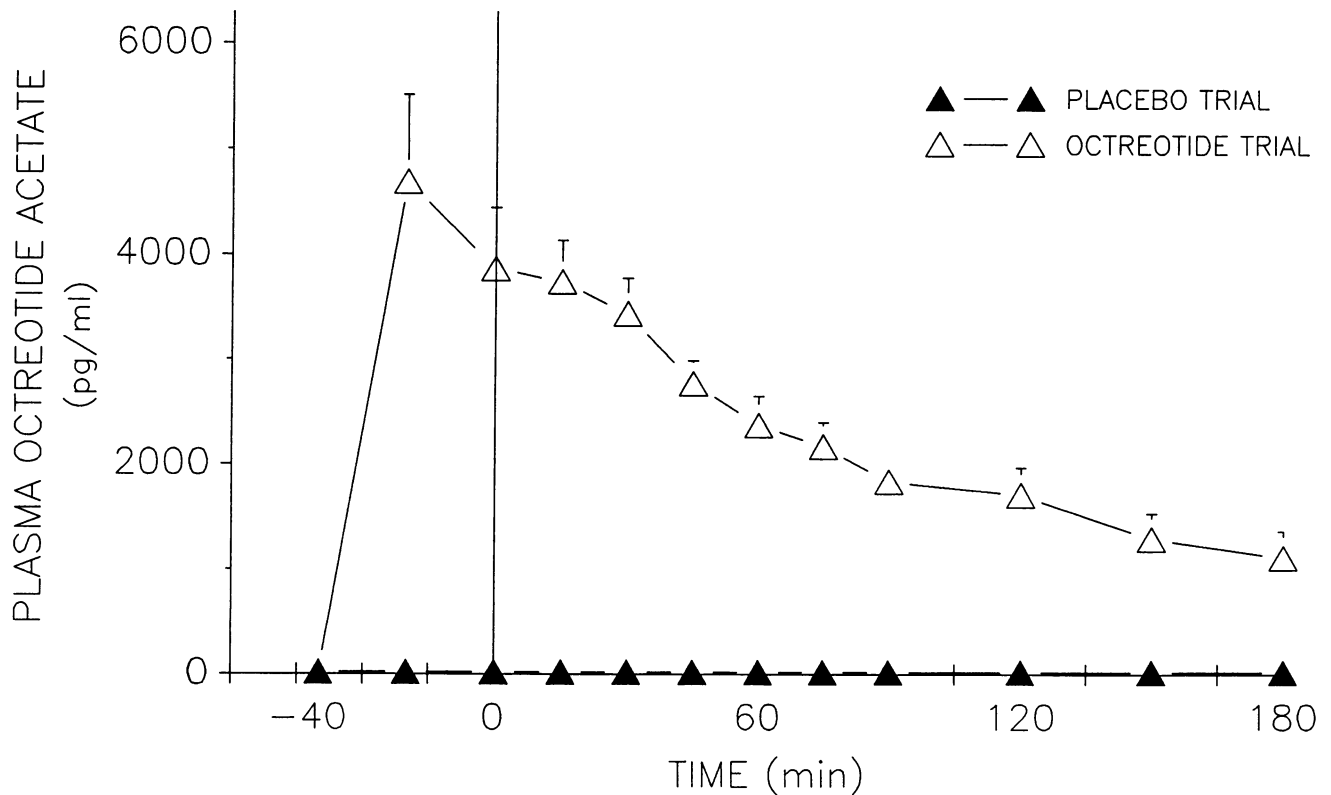


FIG. 6. Plasma levels of the somatostatin analogue in the subjects pretreated with octreotide and receiving a high carbohydrate meal, as described in Figure 1.

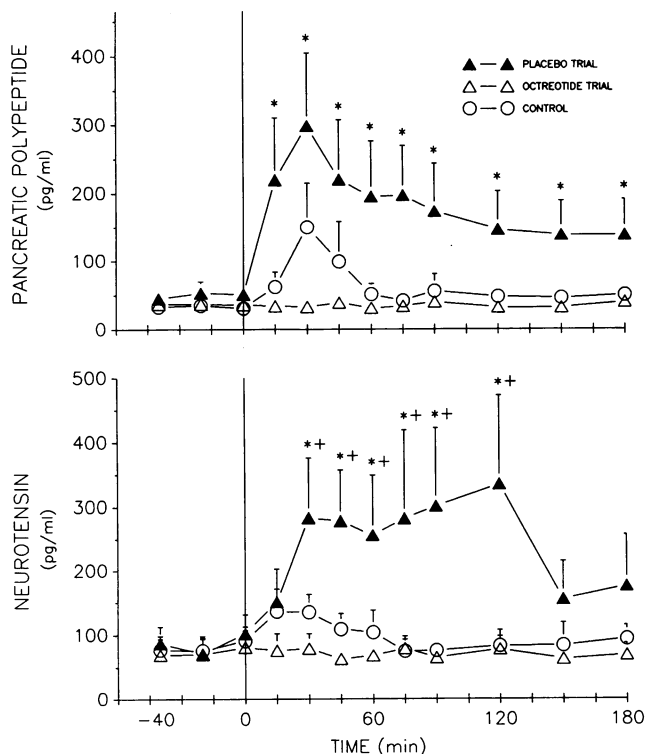


FIG. 7. Plasma levels of pancreatic polypeptide (upper panel) and neurotensin (lower panel) in the same subjects described in Figure 1 while pretreated with octreotide (open triangles) or placebo (closed triangles). (\* Denotes difference between  $\blacktriangle$  and  $\triangle$ ,  $p < 0.01$  and + denotes difference between  $\blacktriangle$  and  $\Delta$ ,  $p < 0.05$ .)

longer half-life (75 to 90 minutes *versus* 1 to 2 minutes), which allows its administration *via* a subcutaneous route. The biologic activity of this analogue is well maintained and compares well to that of cyclic somatostatin.<sup>22</sup> Octreotide acetate had been shown to be effective in a num-

TABLE 2. Gastric Emptying Time ( $t_{1/2}$  in Minutes) in Postgastrectomy Subjects

Patient	Dumping		Nondumping
	Placebo	Octreotide	Controls
3	150	1338	54
4	96	454	246
5	82	174	118
7	33	754	118
10	21	169	93
Mean $\pm$ SEM	76 $\pm$ 23	578 $\pm$ 244*	125 $\pm$ 36

The patients with dumping symptoms were studied twice, with and without pretreatment with octreotide acetate. The control subjects consisted of postgastrectomy patients who did not manifest any dumping symptoms. Gastric emptying was assessed using technetium 99-labeled scrambled eggs.

\* Denotes significance from placebo trial ( $p < 0.05$ ) using paired t test and from control group ( $p < 0.05$ ) using nonparametric t test.

TABLE 3. Effect of Long-term Treatment with Octreotide Acetate on Biochemical Parameters and on Weight Gain

Parameter	Before Treatment	After Treatment	
		3 months (n = 10)	15 months (n = 8)
Glucose (mg/dL)	95 $\pm$ 5	90 $\pm$ 6	99 $\pm$ 4
Total protein (g/dL)	6.6 $\pm$ 0.2	6.6 $\pm$ 0.1	7.6 $\pm$ 0.2
Albumin (g/dL)	3.9 $\pm$ 0.1	3.9 $\pm$ 0.1	4.4 $\pm$ 0.2
Total bilirubin (mg/dL)	0.3 $\pm$ 0.006	0.6 $\pm$ 0.4	0.3 $\pm$ 0.06
Cholesterol (mg/dL)	179 $\pm$ 13	173 $\pm$ 9	215 $\pm$ 7
LDH (I.U.)	192 $\pm$ 17	203 $\pm$ 7	187 $\pm$ 8
SGOT (I.U.)	29 $\pm$ 4	23 $\pm$ 3	22 $\pm$ 2
Weight gain (% of body weight)	—	7.2 $\pm$ 1.2	11 $\pm$ 1.3*

\* Denotes significance from pretreatment and 3-month periods, each at  $p < 0.01$ .

ber of endocrine syndromes, including carcinoid,<sup>23</sup> insulinoma, VIPoma, and glucagonoma.<sup>24</sup>

The data obtained from the present study and another one from this laboratory<sup>25</sup> emphasized the importance of hormones in mediating the symptomatology of early and late dumping. They also indicate that the systemic symptoms of early dumping are unlikely to be related to changes in either plasma vasoactive intestinal peptide, gastrin, or motilin. None of these hormones were altered in the dumping patients during the placebo trial or in the post-gastrectomy nondumping controls. The plasma level of pancreatic polypeptide, neurotensin, and glucagon were markedly elevated during the placebo trial and their levels were suppressed with octreotide pretreatment. It is plausible that these changes implicate a role for these peptides as causative agents in the development of dumping symptoms. However the data obtained in the control group suggest that pancreatic polypeptide does not play a major role in the development of dumping symptoms. The increases in plasma levels of this hormone in response to the breakfast meal in the control group were similar to those seen in the dumping patients while receiving the placebo trial. Furthermore the changes in plasma glucagon also are unlikely to be responsible for the appearance of dumping symptoms in response to the high carbohydrate meal. Glucagon, albeit in pharmacologic doses, is known to decrease gastrointestinal motility and to result in atony.<sup>26</sup> Taken together our data suggest that neurotensin plays a major role in the development of the dumping syndrome. Neurotensin was shown to influence gastrointestinal motility of both the upper and lower intestinal



tracts.<sup>27</sup> Infusion of this hormone in humans also was shown to increase the intestinal motility index of the colon and result in diarrhea.<sup>28</sup>

Several other causative agents, not measured in the present study, also were implicated in the development of the syndrome, including kallikrein<sup>29</sup> and serotonin.<sup>7,8</sup> The problem with isolating all of these factors lies in our ability to measure the site at which they exert their biologic activity. In this and other studies, the changes in plasma hormones were measured in the peripheral circulation. This, however, does not preclude the possibility that the symptoms of dumping may be directly related to the actions of gastrointestinal peptides *via* paracrine, autocrine, neural, or luminal routes. More conclusive evidence for implicating any of the above factors will have to await further trials, in which the development of symptoms is monitored during the infusion of such agents, singly or in combination, or when their endogenous secretions are either selectively stimulated or blocked.

The exact mechanism by which octreotide acetate improved the early symptoms of dumping remains unclear. Recent evidence suggests that the peptide-inhibitory effect of octreotide acetate results in a delay in the upper gastrointestinal motility.<sup>30</sup> Octreotide acetate has been shown to decrease the frequency and amplitude (motility index) of contractions in the gastric remnant and in the attached proximal small bowel. In addition it changes the motility of the upper gastrointestinal tract from a fed to a fasted pattern.<sup>25</sup> These changes can thus result in a delay in gastric emptying, which, in turn, is expected to retard the transit of the hyperosmolar meal from the gastric remnant into the small intestine, thus preventing the initiation of dumping. The overall effects lead to decreased incidence of abdominal cramps, borborygmi, intestinal hurry, and diarrhea. The improvement in the two patients with late dumping symptoms can be attributed to the effects of octreotide acetate in preventing the increase in plasma insulin in response to the high carbohydrate meal. This, in turn, prevented the development of late-onset reactive hypoglycemia.

Long-term treatment of patients with severe dumping symptoms, using three to four daily injections of octreotide acetate, was very gratifying. Subjectively all of the patients reported continued diminution of symptoms while using the lowest possible effective dose given 30 minutes before each meal. Seven patients who were crippled by their symptoms before treatment have now returned to full- or part-time employment. The use of this drug has enabled patients to no longer dread travel outside their homes for fear of disabling diarrhea. Weight gain occurred in all patients, which confirms the subjective reports given by these patients. There were no adverse effects noted with long-term treatment with the analog

during a 15-month period. Three patients on octreotide acetate treatment complained of diarrhea shortly after awakening in the morning. This was relieved by administering a dose of the analog immediately before bedtime.

A double-blind prospective trial has shown that octreotide acetate is remarkably effective in the acute treatment of early and late symptoms in patients with severe postgastrectomy dumping syndrome. Long-term treatment was successful and, most importantly, had no major side effects. The mechanism of action of this analog appears to be a reduction of the gastrointestinal motility, probably mediated by inhibition of the release of several humoral agents, most notably neurotensin.

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